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Expression and Possible Role of NMDA Receptor Channel in C2C12 Skeletal Muscle Myoblasts

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N-methyl-D-aspartate (NMDA) receptor channel is important for synaptic plasticity, which is thought to underlie learning and memory. NMDA receptor channel is gated by both ligands and voltage, and is highly permeable to Ca^{2+}. These characteristics of the channel directly relate to its important physiological roles. One of the most prominent events in myogenic differentiation is the fusion of mononucleated myoblasts into multinucleated myotubes, and this myogenic process absolutely requires Ca^{2+} influx. However, little is known about the channels that are responsible for the entry of Ca^{2+} into the cells. Here we show that NMDA receptor channel is involved in Ca^{2+} influx during myogenesis. Upon analysis of gene expression in C2C12 mouse myoblast cell line, NMDA receptor channel subunits are highly expressed in the differentiating cells. Agonists of NMDA receptor channel enhanced myoblast fusion, while antagonist and antisense oligonucleotide of that inhibited the fusion. Furthermore, this inhibition of the fusion could be effectively reversed by treatment of ionomycin. These results suggest that NMDA receptor channel is likely to be involved in Ca^{2+} influx that is a prerequisite for membrane fusion of myogenic cells.

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A Role of Tyrosine Phosphorylation in the Skeletal Muscle Differentiation

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Signal transduction cascades that are driven by tyrosine phosphorylation regulate cell proliferation and differentiation. The initiation, extent, and termination of tyrosine phosphorylation is determined by the concerted activities of protein tyrosine kinases (PTKs) and protein tyrosine phosphatases (PTPases). The myogenesis is accompanied by the fusion of mononucleated myoblasts into multinucleated myotubes and is regulated by growth factors whose signal is transmitted through tyrosine phosphorylation. However, little is known about signal transduction pathway driven by tyrosine phosphorylation in myogenesis. To examine whether the regulation of tyrosine phosphorylation is implicated in myogenesis, myogenic cell lines were treated with vanadate, an inhibitor of PTPase. Vanadate stimulated myoblast fusion, and this stimulating effect of vanadate was synergistically enhanced by the combination with hydrogen peroxide, mimetics of vanadate in insulin action. On the other hand, genistein, an inhibitor of PTK, inhibited myoblast fusion. These results suggest that tyrosine phosphoylation is one of the key regulation steps in myogenic differentiation.